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Committee on Energy and Commerce
Subcommittee on Health

Committee Prints on Administration Legislative Proposals on the Animal Drug User Fee Act Amendments of 2008 and the Animal Generic User Fee Act of 2008

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Mr. Chairman and members of the Subcommittee:

Thank you for holding this hearing on this important piece of legislation, and for the opportunity to speak to you today about the important human and animal health benefits that result from using medicines to keep animals healthy.

I am Dr. Richard Carnevale. I am a veterinarian by training with a degree from the University of Pennsylvania and I am here today on behalf of the Animal Health Institute, a trade association that represents companies that make medicines for animals. Our companies share a common mission: we contribute to public health by protecting animal health. With food animals in more demand from our growing global population, the importance of the nexus between animal health and human health has never been greater, and is one of the driving forces behind the Center for Disease Control's "One Health" initiative. Recent highly-publicized threats like avian influenza highlight this nexus. As companion animals have become a more important part of our everyday lives they have moved from the backyard into our living rooms and bedrooms, increasing their importance to humans and requiring greater attention to their health needs. As medical breakthroughs from human medicine are adapted to animal medicine, our pets are living longer and healthier lives.

Animal health products also give veterinarians, and livestock and poultry producers, the necessary tools to protect the health and well-being of food producing animals. More and more evidence demonstrates that a vital first step in producing safe meat, milk and eggs is keeping animals healthy. Veterinarians work hard to prevent disease in animals, but it is important for them to have medicines available when needed to treat a disease.

The statutory standard for FDA approval of animal drugs under the Federal Food, Drug and Cosmetic Act is the same as that for human drugs: they must be proven to be safe and effective. As a result, the animal drug approval process looks much like the human drug approval process: animal drug companies submit data packages to demonstrate safety, efficacy, and the ability to meet the same stringent FDA manufacturing standards. It is a costly process, requiring as much as $100 million and 7-10 years to bring an animal drug to market. In the case of food animals, the standard to ensure that meat, milk, and

eggs are safe for human consumption adds an additional set of requirements that increases the cost and time to market.

The market for animal drugs, however, is nothing like the market for human drugs. Our products are used to treat seven different major species of animals and many more minor species. A blockbuster animal drug will have sales of $100 million, and the vast majority of animal health products have a market size of around $1 million. There is no Medicare or Medicaid and, except in rare cases, no employer supported health insurance -- the cost of animal drugs is borne in full by the animal owner.

Animal health companies rely on a rigorous, efficient, predictable and science-based review process at the Food and Drug Administration's Center for Veterinary Medicine (CVM) to provide these products. That's why our companies supported the first authorization of the Animal Drug User Fee Act more than five years ago. The Animal Drug User Fee Act of 2003 (ADUFA I) made it possible for our companies to bolster funding at CVM so that they could meet performance standards to improve the efficiency and predictability of the animal drug approval process.

As a result of an efficient and predictable regulatory process, animal health companies can be more confident investing research dollars in the United States. According to data AHI collects, in 2006 pioneer animal health companies invested $663 million in research and development of new and innovative products, a seven percent (7%) increase over the preceding year.

We believe ADUFA I has been successful. The backlog of overdue pioneer animal drug submissions that existed at the beginning of the program is gone. FDA/CVM has successfully met the performance goals established by the legislation. Timeframes have been uniformly met, restoring predictability to the review process. As a testament to this progress, 2007 was a banner year for approval of new and innovative products with CVM approving nine new chemical entities, giving veterinarians new medicines to fight diseases and other conditions in animals. Examples include medicine to treat heart failure in dogs, control pain and inflammation from osteoarthritis and to treat and prevent motion sickness.

The legislation before you to reauthorize this successful program builds upon this record of achievement. Animal health companies approached ADUFA II with the goal of reducing overall review times. CVM came to the table with a need for additional resources to compensate for the gap between the increased employee cost and Congressional appropriations. The end-review amendment process established in this agreement will help reduce the overall review time by reducing the number of submission cycles. The ten agreed upon workshops will help CVM and sponsors deal with the complex scientific questions that often surround the review of these products.

Whereas the total cost of ADUFA I came to around $43 million over five years, sponsors will contribute $98 million to this process over the life of this legislation. The only change in the financial structure is the inflation factor calculated annually during the life of ADUFA I has been agreed to and built into the annual costs of ADUFA II, giving both sponsors and CVM more predictability regarding the program's revenue.

Many will benefit should Congress approve this legislation:

1. FDA/CVM benefits by having additional resources to meet its mission of protecting public health.

2. Animal health sponsors benefit from a stable and predictable review process, allowing them to make informed decisions about the investment risks of research and development dollars.

3. Veterinarians benefit from having new and innovative medical advances available to treat, control and prevent diseases in their patients.

4. Livestock and poultry producers, and the veterinarians on whose advice they rely, also have the tools needed to keep food animals healthy.

5. Pet owners benefit by having their animals live longer and healthier lives, increasing their enjoyment of these companions.

6. Consumers reap the food safety benefits that come as a result of the availability of additional tools to keep food animals healthy.

These widespread benefits are why a broad coalition of companion animal interests and animal agriculture interests support this legislation. Attached to my testimony is a copy of a coalition letter sent to you earlier this year from this broad mix of groups asking for Congressional action on this bill.

<u>Protections in Place to Protect Public Health</u>

We would like to emphasize that the regulatory process this bill will support is one of the most protective of human health in the world. This bill does not in any way alter or change the rigorous pre- and post-approval animal safety and food safety standards. FDA/CVM's has a rigorous and robust approval process that takes into account safety throughout the lifecycle of the product, including safety to the animal, safety to humans, a thorough process for measuring the potential transfer of antimicrobial resistant bacteria between animals and humans, environmental safety, animal handler safety and drug experience reporting and adverse reaction evaluation to assess post-market safety.

We strongly believe this bill intensifies CVM's public health focus by increasing the resources used to meet that mission. The timely availability of animal medicines approved by FDA protects public health. A process that is cumbersome and inefficient delays those products that are safe and effective and encourages the use of untested and illegally compounded products in an attempt to address unmet animal health needs. These types of treatments can create a health hazard for the animals and jeopardize food safety. Increasing agency resources and setting achievable timeframes will only help improve the agency's ability to meet its high safety standards.

The rigorous review process and monitoring systems in place are at the heart of a broad system of protections that ensure that all medicines, including antibiotics, are safe for animals and humans. Antibiotics for use in animals must meet all the same requirements as antibiotics used in humans, with two additional requirements: first, sponsors must show the meat from animals in which the product is used is safe for human consumption. Second, beginning in 2003, CVM instituted Guidance for Industry

(GFI) # 152, which outlines a qualitative risk assessment process that is applied to all antibiotics approved for use in animals. This guidance process is designed to measure the risk of antibiotic resistant bacteria being transferred from animals to humans if the product is approved. Based on this risk, FDA makes decisions to either deny or approve the produce with certain restrictions to significantly reduce risk. Restrictions can include requiring a veterinary prescription, prohibiting extra-label use and prohibiting use in certain species. The methodology is very conservative – meaning it is very difficult to get an antibiotic approved. Further, the guidance is sufficiently broad so that if new, previously unidentified or undescribed, resistant organisms or genes were to become of concern, the Agency can act swiftly to take this information into account. The existing guidance allows the Agency sufficient flexibility to allocate resources appropriately to changing issues of safety related to resistance emergence.

The GFI # 152 process applies not only to new submissions, but to all existing products as well. FDA has established a priority list for the re-evaluation of all antibiotics currently approved and marketed. Most of the drugs on the list are antibiotics administered in animal feed for the prevention and control of animal diseases or to increased the weight gains and improve feed efficiency. The re-review under Guidance 152 was stimulated by new funding that FDA received and continues to receive via annual appropriated money specifically earmarked for these reviews. Bear in mind, though, the evaluation of these products did not begin with Guidance 152. In response to concerns raised some 30 years ago, the Bureau of Veterinary Medicine in FDA, in the 1970's, required sponsors of these products to conduct tests to determine the potential for resistance to be selected in the animals and to be transferred to bacteria that could cause human disease. While the standards and science may have changed over the years, the safety of these products has been an ongoing exercise at FDA. Moreover, published quantitative risk assessments performed by both the agency and individual product sponsors have generally affirmed that the risks to human health from these antibiotics in animal feed under approved conditions of use are quite low.

We fully support efforts by the agency to continue to evaluate the safety of these products using all available scientific data under a sound risk assessment approach in order the determine the true risk to public health and guide appropriate risk management interventions to protect public health.

In addition to the rigorous review process and the additional public and private risk assessments that have been conducted, there are other post-approval layers of protection to ensure the safe use of antibiotics.

<u>Monitoring programs</u>

USDA's Food Safety and Inspection Service monitor meat samples for the presence of antibiotic residues as a check on the observance of the withdrawal times set by FDA. It is very uncommon for FSIS to find a violative residue, an indication that products are being used according to label directions.

The National Antimicrobial Resistance Monitoring System (NARMS) is a multi-agency program coordinated by FDA to monitor the possible emergence of antibiotic resistant bacteria and allow for implementation of management and control measures if needed. The three agencies involved are:

- The USDA Agricultural Research Service (ARS), which collects samples from slaughter and processing facilities to monitor for antibiotic resistance trends in farm animals.
- The FDA, which monitors for resistant bacteria in retail meats;
- The Centers for Disease Control and Prevention (CDC), which collects isolates, or samples, from public health laboratories to monitor for the emergence of antibiotic resistant food-borne pathogens in humans;

To date, the program has produced seven years of data representing over 50,000 animals and 11,000 human *Salmonella* isolates. Most bacterial species isolated from humans and tested for resistance against drug classes potentially related to animal usage have shown stable or declining resistance patterns. Most of the multiple-drug resistance types, such as *Salmonella typhimurium* DT104 show stable or declining prevalence in both food animals and humans since 1996, according to an expert report issued in 2006 by the Institute of Food Technologists entitled "Antimicrobial Resistance: Implications for the Food System."

Judicious use principles

Responsible, or judicious, use programs that are specific to different livestock species give veterinarians and producers specific guidelines to help them safely and properly use of antibiotics in their health management systems. Generally, these guidelines have been prepared collaboratively by FDA, CDC and veterinary groups.

There remains a great deal of confusion about how antibiotics are used in animal agriculture. CVM approves these products for four specific purposes:

1. Disease treatment
2. Disease prevention
3. Disease control
4. Growth promotion, as measured by the amount of feed needed to produce a pound of animal weight or increased rate of weight gain.

Many assume in-feed uses equate to growth promotion, but this confuses the use with the route of administration. In fact, any of the four uses can be administered via feed, as that is the only practical way to administer medication to large flocks or herds. In most cases, a veterinarian is involved in this process, recommending feed that is specifically formulated for the health management system used for the flock or herd.

Perhaps the most discussed, and most misunderstood use, is the growth promotion use. The Animal Health Institute collects annual data from its members on the amount of antibiotics sold for use in animals. As part of that survey, we ask members to estimate the amount sold that is used for growth

promotion. In 2006, that amount was 4.6 percent of the total. Each year we publically release the results of this survey, and a copy of the 2006 results is attached to my testimony.

There is one other note about growth promotion: when the European Union phased out the use of antibiotics for growth promotion, according to data from the Danish government, animal death and disease rose, requiring a greater amount of antibiotics to be used to treat disease. Clearly, as has been discussed in many peer-reviewed articles, this use also had the effect of suppressing disease that did not necessarily produce symptoms.

Mr. Chairman, CVM has a rigorous, science-based approval process that provides to the American public the products necessary to protect public health by protecting animal health. Every year scientists uncover new diseases in animals, some of which potentially pose a threat to human health. As more animals are raised to feed the planet and as animals are reared closer to people, we will continue to need new medicines to protect animal and human health.

The reauthorization of ADUFA will continue to provide the agency the resources necessary to maintain and improve this approval process, provide new and innovative products to allow our pets to live longer and healthier lives and contribute to food safety by keeping food animals healthy. I urge you to move a clean ADUFA bill in a timely manner so this program can continue without interruption.